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☐	L20	L19 and Tie	2
☐	L19	L16 and ligand	36
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☐	L16	L15 and endocrine	38
☐	L15	L13 and VEGF	118
☐	L14	L13 and EG-VEGF	0
☐	L13	530/300.ccls.	3717
☐	L12	L11 and EG-VEGF	3
☐	L11	(wood)adj(william)	3208
☐	L10	L9 and EG-VEGF	3
☐	L9	(watanabe)adj(colin)	1613
☐	L8	L7 and EG-VEGF	5
☐	L7	L6 and VEGF	413
☐	L6	(ferrara)adj(napoleone)	457
☐	L5	(ferrara)adj(neopoleone)	0
☐	L4	(EG-VEGF)	27
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L2 ANSWER 1 OF 39 CAPLUS COPYRIGHT 2005 ACS on STN
2005:902707 Document No. 143:246742 Chimeric immunogens employing VEGF and helper T-cell peptide epitopes. Kaumaya, Pravin; Cohn, David (The Ohio State University Research Foundation, USA). PCT Int. Appl. WO 2005076972 A2 20050825, 65 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IS, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2005-US3747 20050207. PRIORITY: US 2004-2004/PV542041 20040205.

AB The authors disclose compns. and methods of treating patients with malignancies associated with overexpression of VEGF, particularly ovarian cancer. In one example, the compns. comprise VEGF epitopes and chimeric peptides comprising one or more of said epitopes and a T cell epitope.

L2 ANSWER 2 OF 39 CAPLUS COPYRIGHT 2005 ACS on STN
2005:523320 Document No. 143:53487 Treatment of rheumatoid arthritis with hypoxia-inducible factor 1α antagonists. Defranoux, Nadine; Hurez, Vincent Jacques; Michelson, Seth G.; Shoda, Lisl Katharine; Wennerberg, Leif Gustaf (Entelos, Inc., USA). PCT Int. Appl. WO 2005053744 A1 20050616, 72 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IS, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2004-US39484 20041124. PRIORITY: US 2003-2003/PV525363 20031126.

AB The invention encompasses a novel method of treating inflammatory disease, such as rheumatoid arthritis, and novel methods of identifying and screening for drugs useful in the treatment of inflammatory diseases and their clin. symptoms. The inventors have made the discovery that the activity of HIF-1α, a transcription regulator known to have an effect on some cancers, has a significant impact on the pathophysiol. of rheumatoid arthritis. The symptoms of an inflammatory disease, such as rheumatoid arthritis, may be alleviated by administering a compound that inhibits the activity of HIF-1α.

L2 ANSWER 3 OF 39 MEDLINE on STN DUPLICATE 1
2005031952. PubMed ID: 15483093. Localization and quantification of cyclic

changes in the expression of endocrine gland vascular endothelial growth factor in the human corpus luteum. Fraser Hamish M; Bell Julie; Wilson Helen; Taylor Paul D; Morgan Kevin; Anderson Richard A; Duncan W Colin. (Medical Research Council Human Reproductive Sciences Unit, Centre for Reproductive Biology, Edinburgh, Scotland, United Kingdom.. h.fraser@hrsu.mrc.ac.uk) . Journal of clinical endocrinology and metabolism, (2005 Jan) 90 (1) 427-34. Electronic Publication: 2004-10-13. Journal code: 0375362. ISSN: 0021-972X. Pub. country: United States. Language: English.

AB Angiogenesis is essential for normal growth and function of the corpus luteum. The roles of various angiogenic factors in these events are being elucidated. Endocrine gland vascular endothelial growth factor (**EG-VEGF**) has recently been described in the human ovary. To define the localization of **EG-VEGF** mRNA in the corpus luteum and determine changes in its expression, dated human corpora lutea were studied at the early, mid-, and late luteal phases. Quantitative RT-PCR was employed to determine changes in **EG-VEGF** mRNA and compare expression to its related factor prokineticin-2 and the established angiogenic factor, VEGF. In situ hybridization was used to localize sites of production of **EG-VEGF.** To investigate whether expression of **EG-VEGF** was under the influence of LH or progesterone, luteinized granulosa cells were stimulated with human chorionic gonadotropin in the presence or absence of a progesterone synthesis inhibitor. **EG-VEGF** mRNA increased throughout the luteal phase, whereas there was no change in VEGF mRNA. The relative abundance of RNAs based upon PCR signal intensity showed that VEGF and **EG-VEGF** were highly expressed, whereas expression of prokineticin-2 was low. **EG-VEGF** mRNA was localized predominantly to granulosa-derived cells of the corpus luteum. Human chorionic gonadotropin stimulated both VEGF and **EG-VEGF** mRNA in vitro, but the level of expression was not influenced by progesterone. These results establish that in the human corpus luteum **EG-VEGF** is principally derived from granulosa lutein cells and that its synthesis is highest during the mid- to late luteal phase.

L2 ANSWER 4 OF 39 MEDLINE on STN DUPLICATE 2

2005393221. PubMed ID: 15908459. PK1/**EG-VEGF** induces monocyte differentiation and activation. Dorsch Marion; Qiu Yubin; Soler Dulce; Frank Nita; Duong Thao; Goodearl Andrew; O'Neil Steve; Lora Jose; Fraser Christopher C. (Millennium Pharmaceuticals Inc., 35 Landsdowne St., Cambridge, MA 02139, USA.) Journal of leukocyte biology, (2005 Aug) 78 (2) 426-34. Electronic Publication: 2005-05-20. Journal code: 8405628. ISSN: 0741-5400. Pub. country: United States. Language: English.

AB Macrophages exist as sentinels in innate immune response and react by expressing proinflammatory cytokines and up-regulating antigen-presenting and costimulatory molecules. We report a novel function for prokineticin-1 (PK1)/endocrine gland-derived vascular endothelial growth factor. Screening of murine tissue sections and cells for specific binding site leads to the identification of macrophages as an in vivo cellular target for PK1. We demonstrate PK1 induces differentiation of murine and human bone marrow cells into the monocyte/macrophage lineage. Human peripheral blood monocytes respond to PK1 by morphological changes and down-regulation of B7-1, CD14, CC chemokine receptor 5, and CXC chemokine receptor 4. Monocytes treated with PK1 have elevated interleukin (IL)-12 and tumor necrosis factor alpha and down-regulated IL-10 production in response to lipopolysaccharide. PK1 induces a distinct monocyte-derived cell population, which is primed for release of proinflammatory cytokines that favor a T helper cell type 1 response.

L2 ANSWER 5 OF 39 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN

2005:899306 The Genuine Article (R) Number: 946EX. Pattern of endocrine gland-derived vascular endothelial growth factor (**EG-VEGF**)/prokineticin-1 mRNA expression in bovine ovaries throughout

the estrous cycle: More than angiogenic factor.. Kisliouk T (Reprint); Podlovni H; Zhou Q Y; Meidan R. Hebrew Univ Jerusalem, IL-76100 Rehovot, Israel; Univ Calif Irvine, Irvine, CA USA. BIOLOGY OF REPRODUCTION (2005) Sp. iss. SI, pp. 187-187. ISSN: 0006-3363. Publisher: SOC STUDY REPRODUCTION, 1603 MONROE ST, MADISON, WI 53711-2021 USA. Language: English.

L2 ANSWER 6 OF 39 CAPLUS COPYRIGHT 2005 ACS on STN
2004:780858 Document No. 141:273369 Compositions comprising human and mouse Bv8 and **EG-VEGF** with hematopoietic and immune activity and therapeutic uses for blood diseases and immune disorders. Ferrara, Napoleone; Lecouter, Jennifer (Genentech, Inc., USA). PCT Int. Appl. WO 2004081229 A2 20040923, 161 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2004-US7622 20040312. PRIORITY: US 2003-2003/PV45446U 20030312; US 2003-2003/PV511390 20031014.
AB The present invention relates to the novel expression and activities of Bv8 and **EG-VEGF** in hematopoietic stem cells (HSCs), lineage-committed blood progenitor cells, and lymphocytes. In particular, Bv8, **EG-VEGF**, and their receptors are expressed in bone marrow HSCs, peripheral blood leukocytes (PBLs), as well as many hematol. malignant cell lines. Bv8 and **EG-VEGF** are capable of promoting colony formation of bone marrow mononuclear cells and spleen-derived progenitor cells, increasing populations of white blood cells, and promoting activation of B lymphocytes and T lymphocytes. BvS8 nucleic acids and polypeptides, **EG-VEGF** nucleic acids and polypeptides, or combinations thereof can be used in a number of assays and in diagnosis and treatment of conditions associated with hematopoiesis, neutropenias, immunodeficiency disorders, and autoimmune disorders.

L2 ANSWER 7 OF 39 CAPLUS COPYRIGHT 2005 ACS on STN
2004:75976 Document No. 140:139512 **EG-VEGF** receptor antagonists, therapeutic and diagnostic methods, and antagonist identification test system. Haendler, Bernard; Hess-Stumpp, Holger; Schmidt, Anja (Schering A.-G., Germany). Ger. Offen. DE 10229379 A1 20040129, 13 pp. (German). CODEN: GWXXBX. APPLICATION: DE 2002-10229379 20020626.
AB The invention discloses the pharmaceutical use of inhibitors of **EG-VEGF**-polypeptide and **EG-VEGF**-nucleic acid and/or the corresponding receptors for treatment and diagnosis of endometriosis and endometrial carcinoma and for treatment of dysfunctional bleeding. The invention further discloses the use of **EG-VEGF** analogs to increase fertility rates. The invention also discloses a test system for identification of **EG-VEGF** receptor antagonists.

L2 ANSWER 8 OF 39 MEDLINE on STN DUPLICATE 3
2004599383. PubMed ID: 15548611. Bv8 and endocrine gland-derived vascular endothelial growth factor stimulate hematopoiesis and hematopoietic cell mobilization. LeCouter Jennifer; Zlot Constance; Tejada Max; Peale Franklin; Ferrara Napoleone. (Department of Physiology, Genentech, Inc., South San Francisco, CA 94080, USA.. lecouter@gene.com) . Proceedings of the National Academy of Sciences of the United States of America, (2004 Nov 30) 101 (48) 16813-8. Electronic Publication: 2004-11-17. Journal code: 7505876. ISSN: 0027-8424. Pub. country: United States. Language: English.
AB Bv8 and endocrine-gland-derived VEGF (**EG-VEGF**), or prokineticins, are two highly related, secreted proteins that we previously described as selective angiogenic mitogens. Here we describe

the expression and functional characterization of Bv8 in peripheral blood cells, notably monocytes, neutrophils, and dendritic cells, and in the bone marrow. In human and mouse, the two Bv8 G protein-coupled receptors are expressed in hematopoietic stem cells and specific mature blood cells, including lymphocytes. Bv8 is highly expressed by neutrophils at sites of inflammation and can stimulate migration of monocytes, in a pertussis toxin-sensitive manner. Bv8, or **EG-VEGF** that shares the same receptors, increased numbers of colony-forming units granulocytic and monocytic in cultures of human or mouse hematopoietic stem cells. Systemic in vivo exposure to Bv8 or **EG-VEGF** resulted in significant increases in total leukocyte, neutrophil, and monocyte counts. Additionally, adenovirus (Av)Bv8 or AvEG-VEGF delivered just before 5-fluorouracil injury promoted the survival of hematopoietic cells and enhanced progenitor mobilization. In conclusion, Bv8 can promote survival and differentiation of the granulocytic and monocytic lineages. Bv8 potentially modulates growth, survival, and function of cells of the innate and adaptive immune systems, possibly through autocrine or paracrine signaling mechanisms.

L2 ANSWER 9 OF 39 MEDLINE on STN DUPLICATE 4

2004388609. PubMed ID: 15292351. Human endocrine gland-derived vascular endothelial growth factor: expression early in development and in Leydig cell tumors suggests roles in normal and pathological testis angiogenesis. Samson Michel; Peale Franklin V Jr; Frantz Gretchen; Rioux-Leclercq Nathalie; Rajpert-De Meyts Ewa; Ferrara Napoleone. (Department of Molecular Oncology, Genentech, Inc., South San Francisco, California 94080, USA.) Journal of clinical endocrinology and metabolism, (2004 Aug) 89 (8) 4078-88. Journal code: 0375362. ISSN: 0021-972X. Pub. country: United States. Language: English.

AB Angiogenesis is essential for tumor growth and metastasis. A new human angiogenic mitogen, endocrine gland-derived vascular endothelial growth factor (**EG-VEGF**), has been recently identified; its expression pattern is restricted to endocrine glands, with the highest expression in testis. We used in situ hybridization and newly generated monoclonal antibodies to investigate the expression of **EG-VEGF** in normal human prenatal and adult testis and in 48 human testicular tumors of different subtypes. We found that **EG-VEGF** was expressed from 14 wk until birth in human fetal testis. In the adult testis, **EG-VEGF** was strongly expressed only in Leydig cells. In testicular tumors, **EG-VEGF** was expressed specifically in Leydig cell tumors, whereas germ cell-derived neoplasms, including carcinoma in situ, seminoma, and nonseminomatous germ cell tumors, were negative for this antigen. In contrast, VEGF, another powerful angiogenic factor, was expressed in seminoma, but very weakly in Leydig cell tumors. Interestingly, we found that Leydig cell tumors presented vessel surface density 3.2-fold higher than seminoma. These findings argue that human **EG-VEGF** may play a role in angiogenesis both during the early endocrine development of testis and in the adult testis as well as in Leydig cell tumor growth.

L2 ANSWER 10 OF 39 MEDLINE on STN DUPLICATE 5

2004227967. PubMed ID: 15126581. Differential expression of vascular endothelial growth factor (VEGF), endocrine gland derived-VEGF, and VEGF receptors in human placentas from normal and preeclamptic pregnancies. Chung Jin-Young; Song Yang; Wang Yuping; Magness Ronald R; Zheng Jing. (Departments of Obstetrics and Gynecology, University of Wisconsin, Madison, Wisconsin 53715, USA.) Journal of clinical endocrinology and metabolism, (2004 May) 89 (5) 2484-90. Journal code: 0375362. ISSN: 0021-972X. Pub. country: United States. Language: English.

AB Vascular endothelial growth factor (VEGF) is a potent regulator of placental vascular function. Endothelial dysfunction is a key factor associated with preeclampsia. In this study, we examined expression of VEGF, endocrine gland-derived VEGF (**EG-VEGF**), VEGF receptors 1 and 2 (VEGFR-1 and VEGFR-2), and neuropilin-1 and -2 (NP-1 and

NP-2) in human placentas from women with normal and preeclamptic (PE) pregnancies using quantitative or semiquantitative PCR. We found that total VEGF mRNA expression was increased 2.8-fold ($P < 0.05$), along with increases in mRNA expression of VEGF121, 165, and 189 ($P < 0.05$; 1.7-, 1.9-, and 1.8-fold, respectively) in PE vs. normal placentas. Expression of VEGFR-1 mRNA, but not **EG-VEGF** and the other three VEGF receptors studied, was elevated ($P < 0.05$) 2.7-fold in PE vs. normal placentas. Protein expression of VEGF and its four receptors was determined using Western blot analysis. For VEGF, two major isoforms (VEGF165 and 189) were detected. For VEGFR-1, VEGFR-2, NP-1, and NP-2, one major band was observed at 180, 235, 130, and 130 kDa, respectively. All of these bands were corresponding to their positive controls. Of these five proteins studied, only VEGFR-1 levels were increased ($P < 0.05$; 1.7-fold) in PE placentas. The expression of VEGF and the four VEGF receptors was confirmed using immunohistochemistry. They were primarily present in syncytiotrophoblasts and endothelial cells of villous capillaries and large vessels. Thus, together with previous reports that VEGFR-1 mediates trophoblast function and inhibits VEGF-induced angiogenesis and endothelium-dependent vasodilation, these data suggest that the increased VEGFR-1 expression may alter VEGF- mediated function on trophoblast and endothelial cells in PE placentas.

L2 ANSWER 11 OF 39 MEDLINE on STN DUPLICATE 6

2004133478. PubMed ID: 15026321. Angiogenesis and tumor proliferation/metastasis of human colorectal cancer cell line SW620 transfected with endocrine glands-derived-vascular endothelial growth factor, as a new angiogenic factor. Goi Takanori; Fujioka Masako; Satoh Yoshiki; Tabata Shinsuke; Koneri Kenji; Nagano Hideki; Hirono Yasuo; Katayama Kanji; Hirose Kazuo; Yamaguchi Akio. (Department of Surgery I, Fukui Medical University, 23-3 Matsuoka-cho, Yoshida-gun, Fukui 910-1193, Japan.. tgoi@fmsrsa.fukui-med.ac.jp) . Cancer research, (2004 Mar 15) 64 (6) 1906-10. Journal code: 2984705R. ISSN: 0008-5472. Pub. country: United States. Language: English.

AB Endocrine glands-derived-vascular endothelial growth factor (**EG-VEGF**) was recently cloned as a new angiogenic factor that selectively acts on the endothelium of endocrine gland cells. We evaluated the involvement of **EG-VEGF** in colorectal cancer. The expression of **EG-VEGF** was confirmed in all of the colorectal cancer cell lines. (On the other hand, the expression of **EG-VEGF** mRNA was not detected in colorectal normal mucosae.) Stable **EG-VEGF** infectors of colorectal cancer cell line SW620 were produced, **EG-VEGF** transfectants were implanted into cecum and s.c., and cell proliferation was evaluated. Angiogenesis was evaluated by dorsal air sac method. Liver metastasis was evaluated after the implantation of **EG-VEGF** transfectants into the mouse spleen. Tumor proliferation (cecum, s.c.) was significantly higher in the **EG-VEGF** transfectants than in the control cells. The small vessels were significantly increased in **EG-VEGF** transfectants as compared with those in control cells. Also, liver metastatic ratio was higher in the **EG-VEGF** transfectants than in the control cells. In this study, **EG-VEGF**, a new angiogenic factor, may lead to angiogenesis, promoting cell proliferation and liver metastasis in colorectal cancers. When the **EG-VEGF** gene-overexpressing colorectal cancer cell line that had been treated with phosphorothioate antisense **EG-VEGF** oligonucleotides was injected s.c. into mice, angiogenesis and tumor growth were inhibited. Although the novel angiogenesis factor **EG-VEGF** was not expressed in the normal colorectal mucosa, it was expressed in colorectal cancer cells, which indicates that it is a cancer-specific and possibly tissue-specific angiogenesis factor in the large intestine, and which suggests that it can be targeted by a novel antiangiogenesis therapy.

L2 ANSWER 12 OF 39 MEDLINE on STN DUPLICATE 7

2004095079. PubMed ID: 14984768. **EG-VEGF** and Bv8: a novel family of tissue-restricted angiogenic factors. Ferrara Napoleone; LeCouter Jennifer; Lin Rui; Peale Franklin. (Department of Molecular Oncology, Genentech Inc, South San Francisco, CA 94080, USA.. nf@gene.com) . Biochimica et biophysica acta, (2004 Mar 4) 1654 (1) 69-78. Ref: 82. Journal code: 0217513. ISSN: 0006-3002. Pub. country: Netherlands. Language: English.

AB A novel family of angiogenic mitogens have been recently characterized. Endocrine gland-derived vascular endothelial growth factor (**EG-VEGF**), and the mammalian homologue of Bombina variegata peptide 8 (Bv8), are two highly related endothelial cell mitogens and chemotactic factors with restricted expression profiles and selective endothelial cell activity. These peptides share two cognate G-protein coupled receptors. The expression of human **EG-VEGF** occurs predominantly in steroidogenic glands. Consistent with such an expression pattern, the human **EG-VEGF** gene promoter has a potential binding site for steroidogenic factor (SF)-1, a pivotal element for steroidogenic-specific transcription. In the human ovary, the expression of **EG-VEGF** is temporally and spatially complementary to the expression of VEGF-A, both in the follicular and in the luteal phase, suggesting complementary and coordinated roles of these molecules in ovarian angiogenesis. Also, **EG-VEGF** expression correlates with vascularity in the polycystic ovary syndrome, a leading cause of infertility. Bv8 expression is mainly restricted to the testis. The identification of these tissue-selective angiogenic factors raises the possibility that other secreted molecules with selectivity for the endothelium of other organs exist.

L2 ANSWER 13 OF 39 MEDLINE on STN DUPLICATE 8

2004255671. PubMed ID: 15153419. **EG-VEGF**: a novel mediator of endocrine-specific angiogenesis, endothelial phenotype, and function. Lecouter Jennifer; Lin Rui; Ferrara Napoleone. (Department of Molecular Oncology, Genentech Inc., South San Francisco, California 94080, USA.) Annals of the New York Academy of Sciences, (2004 Apr) 1014 50-7. Ref: 69. Journal code: 7506858. ISSN: 0077-8923. Pub. country: United States. Language: English.

AB Angiogenesis is the focus of therapeutic efforts to promote new vessel development in damaged tissues. Conversely, inhibiting endothelial cell growth and survival is a strategy to treat various proliferative diseases. Much evidence indicates that VEGF is a key mediator of angiogenesis. Recently, a novel angiogenic mitogen with tissue-specific expression and target selectivity was characterized. Human endocrine gland derived vascular endothelial growth factor (**EG-VEGF**) is selectively expressed in steroidogenic glands and promotes growth of endocrine gland endothelium. The identification of tissue-selective angiogenic factors raises the possibility that other secreted molecules in this class exist. The potential advantage of tissue-specific angiogenic therapeutics may be the reduction of systemic side effects. Additionally, these peptides or their receptors may be attractive targets for inhibition in several disorders.

L2 ANSWER 14 OF 39 CAPLUS COPYRIGHT 2005 ACS on STN

2003:633928 Document No. 139:175555 Drug screening for inhibitors of peptide ligands for G-protein-coupled receptors ZAQ and 15E as angiogenesis inhibitors. Ohtaki, Tetsuya; Masuda, Yasushi; Takatsu, Yoshihiro (Takeda Chemical Industries, Ltd., Japan). PCT Int. Appl. WO 2003066860 A1 20030814, 308 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (Japanese). CODEN: PIXXD2. APPLICATION: WO 2003-JP1057 20030203. PRIORITY: JP 2002-27299 20020204.

AB Provided are a method and kit for screening compds. inhibiting the activity of novel peptide ligands for two orphan G-protein-coupled receptors ZAQ and 15E. Such compds., antisense nucleic acids or antibodies, are usable as, for example, angiogenesis inhibitors in diagnosis, prevention, and therapy for cancer, polycystic ovary syndrome, ovary overstimulation, etc. The amino acid sequences of those peptides, human, mouse, rat, and bovine ZAQ ligand peptide, snake venom MITI and human and other mammalian homolog (Bv8 peptide), are provided. Endocrine gland-derived vascular endothelial growth factor (**EG-VEGF**, identical to prokineticin 1) is a novel peptide recently identified as a selective mitogen for endocrine gland endothelial cells. The present study demonstrates that **EG-VEGF** /prokineticin 1 and a peptide closely related to **EG-VEGF** , prokineticin 2, are cognate ligands of two orphan G-protein-coupled receptors designated ZAQ (= **EG-VEGF**/PK-R1) and 15E (= **EG-VEGF**/PK-R2). **EG-VEGF** /prokineticin 1 and prokineticin 2 induced a transient increase in intracellular calcium ion concentration ([Ca2+]i) with nanomolar potency in Chinese hamster ovary (CHO) cells expressing **EG-VEGF** /PK-R1 and -R2 and bind to these cells with high affinity and with different receptor selectivity. **EG-VEGF**/prokineticins provoke rapid phosphorylation of p44/42 MAP kinase and DNA synthesis in the bovine adrenal capillary endothelial cells (BACE). The mRNAs of both **EG-VEGF**/PK-R1 and -R2 were expressed in BACE. The identification of the receptors for **EG-VEGF** /prokineticins may provide a novel mol. basis for the regulation of angiogenesis in endocrine glands.

L2 ANSWER 15 OF 39 MEDLINE on STN DUPLICATE 9

2003379638. PubMed ID: 12915658. Presence and regulation of endocrine gland vascular endothelial growth factor/prokineticin-1 and its receptors in ovarian cells. Kisliouk Tatiana; Levy Nitzan; Hurwitz Arye; Meidan Rina. (Department of Animal Sciences, The Hebrew University of Jerusalem, Rehovot 76100, Israel.) Journal of clinical endocrinology and metabolism, (2003 Aug) 88 (8) 3700-7. Journal code: 0375362. ISSN: 0021-972X. Pub. country: United States. Language: English.

AB Endocrine gland vascular endothelial growth factor (**EG-VEGF**) is a novel angiogenic mitogen selective for endothelial cells (EC) in endocrine glands. **EG-VEGF** is identical to a protein previously cloned and termed prokineticin (PK)-1. The present study examined the expression of **EG-VEGF**/PK-1 and its receptors in ovarian steroidogenic cells and EC and compared the regulation of **EG-VEGF**/PK-1 and VEGF expression in SV40 transformed luteinized human granulosa cell line (SVOG). Normal granulosa or SVOG cells expressed **EG-VEGF**/PK-1 mRNA. Incubation of SVOG cells with forskolin augmented **EG-VEGF**/PK-1 expression in a dose-dependent manner. Chemical hypoxia induced by CoCl(2) and desferrioxamine mesylate (100 micro M each) markedly reduced **EG-VEGF**/PK-1. In contrast, hypoxia significantly elevated VEGF mRNA (VEGF165, 189) and protein secretion. Thrombin, like hypoxia, also induced an opposite effect on VEGF and **EG-VEGF**/PK-1. Whereas **EG-VEGF**/PK-1 and VEGF were inversely regulated, steroidogenesis and **EG-VEGF**/PK-1 were positively correlated in SVOG cells. A distinct pattern of ovarian PK receptor (PK-R) expression was observed in which steroidogenic cells predominantly express PK-R1 receptors, whereas corpus luteum-derived EC express high levels of both PK-R1 and PK-R2. Therefore, acting via either PK-R2 or PK-R1, **EG-VEGF**/PK-1 may have angiogenic as well as nonangiogenic functions in the ovary.

L2 ANSWER 16 OF 39 MEDLINE on STN DUPLICATE 10

2003106208. PubMed ID: 12604792. The endocrine-gland-derived VEGF homologue Bv8 promotes angiogenesis in the testis: Localization of Bv8 receptors to endothelial cells. LeCouter Jennifer; Lin Rui; Tejada Max; Frantz Gretchen; Peale Franklin; Hillan Kenneth J; Ferrara Napoleone.

(Department of Molecular Oncology, Genentech, Inc., South San Francisco, CA 94080, USA.) Proceedings of the National Academy of Sciences of the United States of America, (2003 Mar 4) 100 (5) 2685-90. Electronic Publication: 2003-02-25. Journal code: 7505876. ISSN: 0027-8424. Pub. country: United States. Language: English.

AB We recently identified an angiogenic mitogen, endocrine-gland-derived vascular endothelial growth factor (**EG-VEGF**), with selective activity for endothelial cells of endocrine tissues. Here we describe the characterization of a highly related molecule, Bv8, also known as prokineticin-2. Human Bv8 shares 60% identity and 75% similarity with **EG-VEGF**. The human and mouse Bv8 genes share a common structure. Like **EG-VEGF**, Bv8 is able to induce proliferation, survival and migration of adrenal cortical capillary endothelial cells. Bv8 gene expression is induced by hypoxic stress. Bv8 expression occurs predominantly in the testis and is largely restricted to primary spermatocytes. Adenoviral delivery of Bv8 or **EG-VEGF** to the mouse testis resulted in a potent angiogenic response. We have localized the expression of the Bv8EG-VEGF receptors within the testis to vascular endothelial cells. The testis exhibits relatively high turnover of endothelial cells. Therefore, Bv8 and **EG-VEGF**, along with other factors such as VEGF-A, may maintain the integrity and also regulate proliferation of the blood vessels in the testis.

L2 ANSWER 17 OF 39 MEDLINE on STN DUPLICATE 11

2003223990. PubMed ID: 12746324. Mouse endocrine gland-derived vascular endothelial growth factor: a distinct expression pattern from its human ortholog suggests different roles as a regulator of organ-specific angiogenesis. LeCouter Jennifer; Lin Rui; Frantz Gretchen; Zhang Zemin; Hillan Kenneth; Ferrara Napoleone. (Department of Molecular Oncology, Genentech Inc., South San Francisco, California 94080, USA.) Endocrinology, (2003 Jun) 144 (6) 2606-16. Journal code: 0375040. ISSN: 0013-7227. Pub. country: United States. Language: English.

AB We recently described human endocrine gland-derived vascular endothelial growth factor (**EG-VEGF**) as an endothelial cell mitogen with a novel selective activity and an expression pattern essentially limited to steroidogenic glands. Herein we present the identification and characterization of the mouse ortholog. The mouse cDNA and predicted amino acid sequences are, respectively, 86% and 88% identical with the human. Surprisingly, the mouse **EG-VEGF** transcript is predominantly expressed in liver and kidney. A comparison of human and mouse **EG-VEGF** promoter sequences revealed a potential binding site for NR5A1, which is known to be a pivotal element for steroidogenic-specific transcription, in the human but not mouse promoter. In situ hybridization studies localized expression of mouse **EG-VEGF** mRNA to hepatocytes and renal tubule cells. Interestingly, capillary endothelial cells in these sites share several common structural features with those found in steroidogenic glands. Within liver and kidney, **EG-VEGF** receptor expression was largely restricted to endothelial cells. Mouse **EG-VEGF** promoted proliferation and survival of endothelial cells. We propose that mouse **EG-VEGF**, like human **EG-VEGF**, plays a role in regulating the phenotype and growth properties of endothelial cells within distinct capillary beds.

L2 ANSWER 18 OF 39 MEDLINE on STN DUPLICATE 12

2003235306. PubMed ID: 12759245. Differential expression of the angiogenic factor genes vascular endothelial growth factor (VEGF) and endocrine gland-derived VEGF in normal and polycystic human ovaries. Ferrara Napoleone; Frantz Gretchen; LeCouter Jennifer; Dillard-Telm Lisa; Pham Thinh; Draksharapu Aparna; Giordano Thomas; Peale Franklin. (Department of Molecular Oncology, Genentech Incorporated, South San Francisco, California 94080, USA.) American journal of pathology, (2003 Jun) 162 (6) 1881-93. Journal code: 0370502. ISSN: 0002-9440. Pub. country: United States. Language: English.

AB Angiogenesis is a key aspect of the dynamic changes occurring during the normal ovarian cycle. Hyperplasia and hypervascularity of the ovarian theca interna and stroma are also prominent features of the polycystic ovary syndrome (PCOS), a leading cause of infertility. Compelling evidence indicated that vascular endothelial growth factor (VEGF) is a key mediator of the cyclical corpus luteum angiogenesis. However, the nature of the factor(s) that mediate angiogenesis in PCOS is less clearly understood. Endocrine gland-derived (**EG**)-**VEGF** has been recently identified as an endothelial cell mitogen with selectivity for the endothelium of steroidogenic glands and is expressed in normal human ovaries. In the present study, we compared the expression of **EG-VEGF** and VEGF mRNA in a series of 13 human PCOS and 13 normal ovary specimens by in situ hybridization. **EG-VEGF** expression in normal ovaries is dynamic and generally complementary to VEGF expression in both follicles and corpora lutea. A particularly high expression of **EG-VEGF** was detected in the Leydig-like hilus cells found in the highly vascularized ovarian hilus. In PCOS ovaries, we found strong expression of **EG-VEGF** mRNA in theca interna and stroma in most of the specimens examined, thus spatially related to the new blood vessels. In contrast, VEGF mRNA expression was most consistently associated with the granulosa cell layer and sometimes the theca, but rarely with the stroma. These findings indicate that both **EG-VEGF** and VEGF are expressed in PCOS ovaries, but in different cell types at different stages of differentiation, thus suggesting complementary functions for the two factors in angiogenesis and possibly cyst formation.

L2 ANSWER 19 OF 39 MEDLINE on STN DUPLICATE 13
2003206245. PubMed ID: 12728244. The AVIT protein family. Secreted cysteine-rich vertebrate proteins with diverse functions. Kaser Alexandra; Winklmayr Martina; Lepperdinger Gunther; Kreil Gunther. (Current address: Institute of Genetics, University of Salzburg, Hellbrunnerstrasse 34, A-5020 Salzburg, Austria.) EMBO reports, (2003 May) 4 (5) 469-73. Ref: 25. Journal code: 100963049. ISSN: 1469-221X. Pub. country: England: United Kingdom. Language: English.

AB Homologues of a protein originally isolated from snake venom and frog skin secretions are present in many vertebrate species. They contain 80-90 amino acids, 10 of which are cysteines with identical spacing. Various names have been given to these proteins, such as mamba intestinal protein 1 (MIT1), Bv8 (Bombina variegata molecular mass approximately 8 kDa), prokineticins and endocrine-gland vascular endothelial growth factor (**EG-VEGF**). Their amino-terminal sequences are identical, and so we propose that the sequence of their first four residues, AVIT, is used as a name for this family. From a comparison of the sequences, two types of AVIT proteins can be discerned. These proteins seem to be distributed widely in mammalian tissues and are known to bind to G-protein-coupled receptors. Members of this family have been shown to stimulate contraction of the guinea pig ileum, to cause hyperalgesia after injection into rats and to be active as specific growth factors. Moreover, the messenger RNA level of one of these AVIT proteins changes rhythmically in the region of the brain known as the suprachiasmatic nucleus. This shows that members of this new family of small proteins are involved in diverse biological processes.

L2 ANSWER 20 OF 39 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN DUPLICATE 14
2003:395920 Document No.: PREV200300395920. Endocrine gland vascular endothelial growth factor (**EG-VEGF**) regulates preantral follicle growth. Danforth, Douglas R. [Reprint Author]; Arbogast, Laura K. [Reprint Author]; Kaumaya, Pravin T. P. [Reprint Author]; Cohn, David [Reprint Author]; Friedman, Chad I. [Reprint Author]. Department of Obstetrics and Gynecology, Ohio State University, Columbus, OH, USA. Biology of Reproduction, (2003) Vol. 68, No. Supplement 1, pp. 324-325. print.
Meeting Info.: Thirty-sixth Annual Meeting of the Society for the Study of

Reproduction. Cincinnati, OH, USA. July 19-22, 2003. Society for the Study of Reproduction.
CODEN: BIREBV. ISSN: 0006-3363. Language: English.

L2 ANSWER 21 OF 39 MEDLINE on STN DUPLICATE 15
2003461872. PubMed ID: 14522467. **EG-VEGF** and Bv8. a novel family of tissue-selective mediators of angiogenesis, endothelial phenotype, and function. LeCouter Jennifer; Ferrara Napoleone. (Department of Molecular Oncology, Genentech Inc., 1 DNA Way, South San Francisco, CA 94080, USA.) Trends in cardiovascular medicine, (2003 Oct) 13 (7) 276-82. Ref: 80. Journal code: 9108337. ISSN: 1050-1738. Pub. country: United States. Language: English.
AB Angiogenic molecules are the focus of therapeutic efforts to promote new vessel development in ischemic or damaged tissue and, conversely, to inhibit endothelial cell growth and survival in proliferative disease. Two novel angiogenic mitogens have been characterized recently. Endocrine gland-derived vascular endothelial growth factor (**EG-VEGF**) and the mammalian homologue of Bombina variegata peptide 8 (Bv8) are endothelial cell mitogens and chemotactic factors with restricted expression profiles and selective endothelial cell activity. These highly related peptides share two cognate G-protein-coupled receptors that are homologous to the neuropeptide Y receptor. The identification of tissue-selective angiogenic factors raises the possibility that other secreted molecules in this class exist. The potential advantage of tissue-specific angiogenic therapeutics may be the reduction of systemic side effects. Additionally, these peptides or their receptors may be attractive targets for inhibition in several disorders.

L2 ANSWER 22 OF 39 MEDLINE on STN DUPLICATE 16
2003034508. PubMed ID: 12538479. Expression of endocrine gland-derived vascular endothelial growth factor in ovarian carcinoma. Zhang Lin; Yang Nuo; Conejo-Garcia Jose-Ramon; Katsaros Dionyssios; Mohamed-Hadley Alisha; Fracchioli Stefano; Schlienger Katia; Toll Alanna; Levine Bruce; Rubin Stephen C; Coukos George. (Center for Research on Reproduction and Women's Health, University of Pennsylvania, Philadelphia, Pennsylvania 19104, USA.) Clinical cancer research : an official journal of the American Association for Cancer Research, (2003 Jan) 9 (1) 264-72. Journal code: 9502500. ISSN: 1078-0432. Pub. country: United States. Language: English.
AB The first tissue-specific angiogenic molecule, endocrine gland-derived vascular endothelial growth factor (**EG-VEGF**), was identified recently in human ovary, raising hopes of developing tumor type-specific angiogenesis inhibitors. In the present study, we analyzed the expression of **EG-VEGF** mRNA in normal human tissues and ovarian neoplasms by quantitative real-time reverse transcription-PCR. **EG-VEGF** mRNA was expressed in all ovarian neoplasms examined. No significant difference was identified among benign, low malignant potential neoplasms or stage I ovarian cancer, all of which exhibited 2-fold lower mRNA levels compared with normal premenopausal ovaries. **EG-VEGF** mRNA levels further decreased in late stage compared with early stage carcinomas ($P < 0.05$) and were consistently lower in laser capture microdissected tumor islets compared with surrounding stroma. **EG-VEGF** was undetectable by reverse transcription-PCR in 17 established epithelial ovarian cancer cell lines or in cultured human ovarian surface epithelial cells, whereas it was detected in peripheral blood as well as tumor-infiltrating T lymphocytes. Finally, in contrast to VEGF, **EG-VEGF** mRNA levels did not correlate with clinical outcome in advanced ovarian carcinoma. These results suggest that **EG-VEGF** is most likely derived from nonepithelial components of ovarian carcinomas and may play a marginal role in promoting angiogenesis in advanced ovarian carcinoma. We postulate that **EG-VEGF**-targeted antiangiogenic therapy may prove useful in early stage but not in advanced stage ovarian carcinoma.

L2 ANSWER 23 OF 39 MEDLINE on STN DUPLICATE 17

2003245242. PubMed ID: 12768539. Role of adrenocorticotropic hormone in the development and maintenance of the adrenal cortical vasculature. Thomas Michael; Keramidas Michelle; Monchaux Emmanuelle; Feige Jean-Jacques. (INSERM EMI 01-05, Department of Cellular Responses and Dynamics, Commissariat a l'Energie Atomique, 17 Rue des Martyrs, F-38054 Grenoble Cedex 9, France.) Microscopy research and technique, (2003 Jun 15) 61 (3) 247-51. Ref: 52. Journal code: 9203012. ISSN: 1059-910X. Pub. country: United States. Language: English.

AB The adrenal cortex is a highly vascularized endocrine tissue. A dense network of blood capillaries centripetally irrigates the adrenal gland, allowing every endocrine cell to be in contact with an endothelial cell. The pituitary hormone ACTH controls the coordinated development of the vasculature and the endocrine tissue mass. This suggests that paracrine secretions between steroidogenic adrenocytes and capillary endothelial cells participate in the control of adrenocortical homeostasis. Besides its effect on the vascular tone of arteries, ACTH induces the expression of the angiogenic cytokine VEGF-A (vascular endothelial growth factor-A) in primary cultures of adrenocortical cells. This growth factor is a specific mitogen for endothelial cells and is likely to mediate the hormonal control of adrenocortical vascularization through a paracrine mechanism. The newly discovered angiogenic factor **EG-VEGF** (endocrine-gland-derived vascular endothelial growth factor), the expression of which is restricted to endocrine glands and which is preferentially mitogenic for endocrine tissue-derived endothelial cells, is another candidate mediator of great potential interest. Copyright 2003 Wiley-Liss, Inc.

L2 ANSWER 24 OF 39 CAPLUS COPYRIGHT 2005 ACS on STN

2003:449498 Document No. 139:207917 Determination of disulfide bonds in recombinant **EG-VEGF**/prokineticin 1. Ishibashi, Yoshihiro; Kitada, Chieko; Ohtaki, Tetsuya; Masuda, Yasushi; Yamada, Takao; Suenaga, Masato; Fujino, Masahiko (Discovery Research Laboratories I, Pharmaceutical Research Division, Takeda Chemical Industries, Ltd., Tsukuba, 300-4293, Japan). Peptide Science, Volume Date 2002, 39th, 173-176 (English) 2003. CODEN: PSCIFQ. ISSN: 1344-7661. Publisher: Japanese Peptide Society.

AB We determined the disulfide bond structure in recombinant endocrine gland-derived vascular-endothelial growth factor (**EG-VEGF**)/prokineticin 1 using the following chemical methods: (1) cleavage with BrCN, (2) partial reduction with tris(2-carboxyethyl)-phosphine and alkylation with N-ethylmaleimide (NEM) at pH 4.0, and (3) determination of the positions of NEM-modified Cys residues by amino acid sequence anal. The assigned disulfide bonds were Cys7-Cys19, Cys13-Cys31, Cys18-Cys59, Cys-41-Cys67, and Cys61-Cys77, which is the same pattern as that in mamba intestinal toxin 1 (MIT1).

L2 ANSWER 25 OF 39 CAPLUS COPYRIGHT 2005 ACS on STN

2003:449465 Document No. 139:241832 **EG-VEGF**/prokineticins are cognate ligands for two closely related orphan G-protein-coupled receptors. Masuda, Yasushi; Shintani, Yasushi; Yamada, Takao; Hinuma, Shuji; Ohtaki, Tetsuya; Fujino, Masahiko (Discovery Research Laboratories I, Pharmaceutical Research Division, Takeda Chemical Industries, Ltd., Tsukuba, Ibaraki, 300-4293, Japan). Peptide Science, Volume Date 2002, 39th, 49-52 (English) 2003. CODEN: PSCIFQ. ISSN: 1344-7661. Publisher: Japanese Peptide Society.

AB We isolated **EG-VEGF**/prokineticin 1 from bovine milk and identified **EG-VEGF**/prokineticins as cognate ligands of two orphan G-protein-coupled receptors designated **EG-VEGF**/PK-R1 and **EG-VEGF**/PK-R2. Pharmacol. characterization indicated that **EG-VEGF**/prokineticin 1 and prokineticin 2 potently induced a transient increase in intracellular calcium ion concentration ([Ca2+]i) in Chinese hamster ovary (CHO) cells expressing **EG-VEGF**/PK-R1 and-R2 and bound to these cells with high affinity.

L2 ANSWER 26 OF 39 CAPLUS COPYRIGHT 2005 ACS on STN
2002:10528 Document No. 136:65270 Protein and cDNA sequences encoding human **EG-VEGF** protein and methods of use. Ferrara, Napoleone; Watanabe, Colin; Wood, William I. (Genentech, Inc., USA). PCT Int. Appl. WO 2002000711 A2 20020103, 133 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US20116 20010622. PRIORITY: US 2000-2000/PV21363U 20000623; US 2000-2000/PV23097W 20000907; WO 2000-US32678 20001201.

AB The present invention is directed to novel polypeptides designated herein as **EG-VEGF** of human and to nucleic acid mols. encoding those polypeptides. Also provided herein are vectors and host cells comprising those nucleic acid sequences, chimeric polypeptide mols. comprising the polypeptides of the present invention fused to heterologous polypeptide sequences, antibodies which bind to the polypeptides of the present invention and to methods for producing the polypeptides of the present invention. Also provided herein are methods of screening for modulators of **EG-VEGF**. Furthermore, methods and related methods of treatment are described herein which pertain to regulating cellular proliferation and chemotaxis.

L2 ANSWER 27 OF 39 CAPLUS COPYRIGHT 2005 ACS on STN
2002:964996 Document No. 138:33697 Endocrine gland-derived vascular endothelial growth factor nucleic acids and polypeptides and their biological activities and use in drug screening and therapies. Ferrara, Napoleone; Watanabe, Colin; Wood, William I.; Shek, Theresa (USA). U.S. Pat. Appl. Publ. US 2002192634 A1 20021219, 105 pp., Cont.-in-part of U.S. Ser. No. 886,242. (English). CODEN: USXXCO. APPLICATION: US 2001-27603 20011219. PRIORITY: US 1998-PV96146 19980811; WO 1999-US12252 19990602; US 1999-PV145698 19990726; US 1999-380137 19990825; WO 2000-US219 20000105; WO 2000-US4914 20000224; WO 2000-US8439 20000330; US 2000-PV213637 20000623; US 2000-PV230978 20000907; US 2000-709238 20001108; WO 2000-US32678 20001201; US 2001-886242 20010620.

AB The present invention is based on the identification and characterization of a novel, tissue-restricted, growth and differentiation factor that acts selectively on one endothelial cell type. This factor, referred to as endocrine gland-derived vascular endothelial growth factor (**EG-VEGF**), induces proliferation, migration, and fenestrations in capillary endothelial cells derived from endocrine glands, but has no effect on a variety of other endothelial and non-endothelial cell types tested. **EG-VEGF** also induces phosphorylation of kinases involved in cell proliferation or survival, including ERK1, ERK2, Akt, and eNOS. **EG-VEGF** nucleic acids and polypeptides can be used in a number of assays and in diagnosis and treatment of conditions associated with hormone-producing tissue. Also provided herein are vectors and host cells comprising those nucleic acid sequences, chimeric polypeptide mols. comprising the polypeptides of the present invention fused to heterologous polypeptide sequences, antibodies which bind to the polypeptides of the present invention and to methods for producing the polypeptides of the present invention. Also provided herein are methods of screening for modulators of **EG-VEGF**. Furthermore, methods and related methods of treatment are described herein which pertain to regulating cellular proliferation and chemotaxis.

L2 ANSWER 28 OF 39 MEDLINE on STN DUPLICATE 18
2002139189. PubMed ID: 11751915. Characterization of endocrine gland-derived vascular endothelial growth factor signaling in adrenal cortex capillary endothelial cells. Lin Rui; LeCouter Jennifer; Kowalski

Joe; Ferrara Napoleone. (Department of Molecular Oncology, Genentech Inc., South San Francisco, California 94080, USA.) Journal of biological chemistry, (2002 Mar 8) 277 (10) 8724-9. Electronic Publication: 2001-12-20. Journal code: 2985121R. ISSN: 0021-9258. Pub. country: United States. Language: English.

AB Endocrine gland-derived vascular endothelial growth factor (**EG-VEGF**) has been recently identified as a mitogen specific for the endothelium of steroidogenic glands. Here we report a characterization of the signal transduction of **EG-VEGF** in a responsive cell type, bovine adrenal cortex-derived endothelial (ACE) cells. **EG-VEGF** led to a time- and dose-dependent phosphorylation of p44/42 MAPK. This effect was blocked by pretreatment with pertussis toxin, suggesting that G alpha(i) plays an important role in mediating **EG-VEGF**-induced activation of MAPK signaling. The inhibitor of p44/42 MAPK phosphorylation PD 98059 resulted in suppression of both proliferation and migration in response to **EG-VEGF**. **EG-VEGF** also increased the phosphorylation of Akt in a phosphatidylinositol 3-kinase-dependent manner. Consistent with such an effect, **EG-VEGF** was a potent survival factor for ACE cells. We also identified endothelial nitric-oxide synthase as one of the downstream targets of Akt activation. Phosphorylation of endothelial nitric-oxide synthase in ACE cells was stimulated by **EG-VEGF** with a time course correlated to the Akt phosphorylation. Our data demonstrate that **EG-VEGF**, possibly through binding to a G-protein coupled receptor, results in the activation of MAPK p44/42 and phosphatidylinositol 3-kinase signaling pathways, leading to proliferation, migration, and survival of responsive endothelial cells.

L2 ANSWER 29 OF 39 MEDLINE on STN DUPLICATE 19

2003000065. PubMed ID: 12466223. Nociceptive sensitization by the secretory protein Bv8. Negri Lucia; Lattanzi Roberta; Giannini Elisa; Metere Alessio; Colucci Mariantonella; Barra Donatella; Kreil Gunther; Melchiorri Pietro. (Department of Human Physiology and Pharmacology V. Erspamer, University La Sapienza, 00185 Rome, Italy.. lucia.negri@uniroma1.it) . British journal of pharmacology, (2002 Dec) 137 (8) 1147-54. Journal code: 7502536. ISSN: 0007-1188. Pub. country: England: United Kingdom. Language: English.

AB 1 The small protein Bv8, isolated from amphibian skin, belongs to a novel family of secretory proteins (Bv8-Prokineticin family, SWISS-PROT: Q9PW66) whose orthologues have been conserved throughout evolution, from invertebrates to humans. 2 When injected intravenously or subcutaneously (from 0.06 to 500 pmol kg(-1)) or intrathecally (from 6 fmol to 250 pmol) in rats, Bv8 produced an intense systemic nociceptive sensitization to mechanical and thermal stimuli applied to the tail and paws. 3 Topically delivered into one rat paw, 50 fmol of Bv8 decreased by 50% the nociceptive threshold to pressure in the injected paw without affecting the threshold in the contralateral paw. 4 The two G-protein coupled prokineticin receptors, PK-R1 and PK-R2, were expressed in rat dorsal root ganglia (DRG) and in dorsal quadrants of spinal cord (DSC) and bound Bv8 and the mammalian orthologue, **EG-VEGF**, with high affinity. In DSC, PK-R1 was more abundant than PK-R2, whereas both receptors were equally expressed in DRG. IC(50) of Bv8 and **EG-VEGF** to inhibit [(125)I]-Bv8 binding to rat DRG and DSC were 4.1+/-0.4 nM Bv8 and 76.4+/-7.6 nM **EG-VEGF**, in DRG; 7.3+/-0.9 nM Bv8 and 330+/-41 nM **EG-VEGF**, in DSC. 5 In the small diameter neurons (<30 microm) of rat DRG cultures, Bv8 concentrations, ranging from 0.2 to 10 nM, raised [Ca(2+)](i) in a dose-dependent manner. 6 These data suggest that Bv8, through binding to PK receptors of DSC and primary sensitive neurons, results in intense sensitization of peripheral nociceptors to thermal and mechanical stimuli.

L2 ANSWER 30 OF 39 CAPLUS COPYRIGHT 2005 ACS on STN

2002:590599 Document No. 137:346331 Multiple signaling systems are involved in angiogenesis. Shibuya, Masabumi (Division of Genetics, Institute of

Medical Science, University of Tokyo, Japan). Jikken Igaku, 20(8), 1076-1083 (Japanese) 2002. CODEN: JIIGEF. ISSN: 0288-5514. Publisher: Yodosha.

AB A review, on multiple signaling systems in angiogenesis during embryonic development, discussing roles of angiogenic factors/receptors systems (VEGF/VEGF receptors, angiopoietin/Tie2 receptor), ephrin (Eph)-B2-EphB4, **EG-VEGF**, integrins, transcription factors, and other factors in regulation of angiogenesis.

L2 ANSWER 31 OF 39 MEDLINE on STN DUPLICATE 20

2003023758. PubMed ID: 12530695. Endocrine gland vascular endothelial growth factor (**EG-VEGF**) and the hypothesis of tissue-specific regulation of angiogenesis. Ferrara Napoleone; LeCouter Jennifer; Lin Rui. (Department of Molecular Oncology, Genentech Inc., South San Francisco, CA 94080, USA.. nf@gene.com) . Endocrine research, (2002 Nov) 28 (4) 763-4. Journal code: 8408548. ISSN: 0743-5800. Pub. country: United States. Language: English.

L2 ANSWER 32 OF 39 MEDLINE on STN DUPLICATE 21

2002311122. PubMed ID: 12054613. Isolation and identification of **EG-VEGF**/prokineticins as cognate ligands for two orphan G-protein-coupled receptors. Masuda Yasushi; Takatsu Yoshihiro; Terao Yasuko; Kumano Satoshi; Ishibashi Yoshihiro; Suenaga Masato; Abe Michiko; Fukusumi Shoji; Watanabe Takuya; Shintani Yasushi; Yamada Takao; Hinuma Shuji; Inatomi Nobuhiro; Ohtaki Tetsuya; Onda Haruo; Fujino Masahiko. (Pharmaceutical Research Division, Takeda Chemical Industries Ltd., Wadai 10, Tsukuba, Ibaraki 300-4293, Japan.) Biochemical and biophysical research communications, (2002 Apr 26) 293 (1) 396-402. Journal code: 0372516. ISSN: 0006-291X. Pub. country: United States. Language: English.

AB Endocrine gland-derived vascular endothelial growth factor (**EG-VEGF**, identical to prokineticin 1) is a novel peptide recently identified as a selective mitogen for endocrine gland endothelial cells. The present study demonstrates that **EG-VEGF** /prokineticin 1 and a peptide closely related to **EG-VEGF** , prokineticin 2, are cognate ligands of two orphan G-protein-coupled receptors designated ZAQ (=**EG-VEGF**/PK-R1) and I5E (= **EG-VEGF**/PK-R2). **EG-VEGF** /prokineticin 1 and prokineticin 2 induced a transient increase in intracellular calcium ion concentration ([Ca(2+)](i)) with nanomolar potency in Chinese hamster ovary (CHO) cells expressing **EG-VEGF**/PK-R1 and -R2 and bind to these cells with high affinity and with different receptor selectivity. **EG-VEGF** /prokineticins provoke rapid phosphorylation of p44/42 MAP kinase and DNA synthesis in the bovine adrenal capillary endothelial cells (BACE). The mRNAs of both **EG-VEGF**/PK-R1 and -R2 were expressed in BACE. The identification of the receptors for **EG-VEGF** /prokineticins may provide a novel molecular basis for the regulation of angiogenesis in endocrine glands.

L2 ANSWER 33 OF 39 MEDLINE on STN DUPLICATE 22

2003329369. PubMed ID: 12858543. The role of **EG-VEGF** in the regulation of angiogenesis in endocrine glands. LeCouter J; Lin R; Ferrara N. (Department of Molecular Oncology, Genentech, Inc., South San Francisco, California 94080, USA.) Cold Spring Harbor symposia on quantitative biology, (2002) 67 217-21. Ref: 51. Journal code: 1256107. ISSN: 0091-7451. Pub. country: United States. Language: English.

L2 ANSWER 34 OF 39 MEDLINE on STN DUPLICATE 23

2002667065. PubMed ID: 12427552. Molecular cloning and characterization of prokineticin receptors. Soga Takatoshi; Matsumoto Shun ichiro; Oda Tamaki; Saito Tetsu; Hiyama Hideki; Takasaki Jun; Kamohara Masazumi; Ohishi Takahide; Matsushime Hitoshi; Furuichi Kiyoshi. (Molecular Medicine Laboratories, Institute for Drug Discovery Research, Yamanouchi Pharmaceutical Co., Ltd., 21 Miyukigaoka, Ibaraki 305-8585, Tsukuba, Japan.) Biochimica et biophysica acta, (2002 Dec 12) 1579 (2-3) 173-9.

Journal code: 0217513. ISSN: 0006-3002. Pub. country: Netherlands. Language: English.

AB Recent studies have identified two novel biofunctional proteins, termed prokineticin 1/**EG-VEGF** and prokineticin 2, which were mammalian homologues of mamba MIT1 and frog Bv8. Prokineticins have been demonstrated to exert their physiological functions through G-protein coupled receptors (GPCRs). In this study, we report the molecular identification of two endogenous prokineticin receptors, designated PK-R1 and PK-R2, through a search of the human genomic DNA database. PK-R1, locating in chromosome 2, and PK-R2, locating in chromosome 20p13, shared 87% homology, which was an extremely high value among known GPCRs. In functional assays, mammalian cells expressing PK-Rs responded to prokineticins in a concentration-dependent manner. Tissue distribution analysis revealed that expression of PK-R1 was observed in the testis, medulla oblongata, skeletal muscle and skin, while that of PK-R2 showed preferential expression in the central nervous system. The tissue distribution of PK-Rs reported in this paper suggests that the prokineticins play multifunctional roles in vivo.

L2 ANSWER 35 OF 39 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN DUPLICATE 24

2002:446084 Document No.: PREV200200446084. **EG-VEGF** and the hypothesis of tissue-specific regulation of angiogenesis. Ferrara, Napoleone [Reprint author]; LeCouter, Jennifer [Reprint author]; Lin, Rui [Reprint author]. Dept Molecular Oncology, Genentech Inc, South San Francisco, CA, USA. Biology of Reproduction, (2002) Vol. 66, No. Supplement 1, pp. 82. print.
Meeting Info.: 35th Annual Meeting of the Society for the Study of Reproduction. Baltimore, Maryland, USA. July 28-31, 2002.
CODEN: BIREBV. ISSN: 0006-3363. Language: English.

L2 ANSWER 36 OF 39 MEDLINE on STN DUPLICATE 25

2002233229. PubMed ID: 11969366. **EG-VEGF** and the concept of tissue-specific angiogenic growth factors. LeCouter Jennifer; Ferrara Napoleone. (Department of Molecular Oncology, Genentech, 1 DNA Way, South San Francisco, CA 94080, USA.) Seminars in cell & developmental biology, (2002 Feb) 13 (1) 3-8. Ref: 68. Journal code: 9607332. ISSN: 1084-9521. Pub. country: England: United Kingdom. Language: English.

AB The endothelium of the vascular beds is extremely diverse and exquisitely distinct with respect to the specific tissue compartment served by the vessels. The molecular identity and function of the instructive signals that tailor the tissue-specific endothelial phenotype have been largely undefined. Presumably, a complex, integrated network of signals derived from the tissue parenchyma and/or stromal compartments is responsible. Recently, we identified a novel angiogenic mitogen, endocrine-gland-derived vascular endothelial growth factor, **EG-VEGF**, with a selective activity and very distinct expression pattern. Human **EG-VEGF** is expressed by steroid producing cells in the adrenal gland, placenta, testis and ovary, and is a mitogen for endothelial cells derived from these microvascular beds. **EG-VEGF** may represent the first of a novel class of tissue-specific angiogenic factors that function to regulate and fine-tune endothelial cell growth, structural and functional properties. The identification of other selective angiogenic molecules will allow insight into exciting, basic developmental issues and increase our armamentarium of factors for therapeutic angiogenic and anti-angiogenic strategies.

L2 ANSWER 37 OF 39 MEDLINE on STN DUPLICATE 26

2001486108. PubMed ID: 11528470. Identification of an angiogenic mitogen selective for endocrine gland endothelium. LeCouter J; Kowalski J; Foster J; Hass P; Zhang Z; Dillard-Telm L; Frantz G; Rangell L; DeGuzman L; Keller G A; Peale F; Gurney A; Hillan K J; Ferrara N. (Department of Molecular Oncology, Genentech Inc., South San Francisco, CA 94080, USA.)

Nature, (2001 Aug 30) 412 (6850) 877-84. Journal code: 0410462. ISSN: 0028-0836. Pub. country: England: United Kingdom. Language: English.

AB The known endothelial mitogens stimulate growth of vascular endothelial cells without regard to their tissue of origin. Here we report a growth factor that is expressed largely in one type of tissue and acts selectively on one type of endothelium. This molecule, called endocrine-gland-derived vascular endothelial growth factor (**EG-VEGF**), induced proliferation, migration and fenestration (the formation of membrane discontinuities) in capillary endothelial cells derived from endocrine glands. However, **EG-VEGF** had little or no effect on a variety of other endothelial and non-endothelial cell types tested. Similar to VEGF, **EG-VEGF** possesses a HIF-1 binding site, and its expression is induced by hypoxia. Both **EG-VEGF** and VEGF resulted in extensive angiogenesis and cyst formation when delivered in the ovary. However, unlike VEGF, **EG-VEGF** failed to promote angiogenesis in the cornea or skeletal muscle. Expression of human **EG-VEGF** messenger RNA is restricted to the steroidogenic glands, ovary, testis, adrenal and placenta and is often complementary to the expression of VEGF, suggesting that these molecules function in a coordinated manner. **EG-VEGF** is an example of a class of highly specific mitogens that act to regulate proliferation and differentiation of the vascular endothelium in a tissue-specific manner.

L2 ANSWER 38 OF 39 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN DUPLICATE 27

2002013238 EMBASE VEGF and its receptors. Shibuya M.. Dr. M. Shibuya, Division of Genetics, Institute of Medical Science, University of Tokyo, 4-6-1 Shirokane-dai, Minato-ku, Tokyo 108-8639, Japan. Biotherapy Vol. 15, No. 6, pp. 637-643 2001.
Refs: 23.
ISSN: 0914-2223. CODEN: BITPE
Pub. Country: Japan. Language: Japanese. Summary Language: English; Japanese.

ED Entered STN: 20020117

AB The blood circulation system in vertebrates is regulated by the processes of vasculogenesis, angiogenesis (protruding from preexisting vessels) and vascular remodeling. Vascular endothelial growth factor (VEGF-A) and its receptor system have been shown to be the major regulators of proliferation, differentiation and morphogenesis of vascular endothelial cells. The VEGF family includes VEGF-A, -B, -C, -D, -E and PIGF. The VEGF receptor family contains 3 members, Flt-1 (VEGFR-1), KDR/Flk-1 (VEGFR-2) and Flt-4 (VEGFR-3). KDR has a strong tyrosine kinase activity and transduces the major positive signal of VEGF-A, whereas Flt-1 has dual, positive and negative functions, due to its strong VEGF-A trapping activity and a weak kinase activity. The VEGF-C and -D and Flt-4 system regulates lymphatic vessel formation. VEGF and its receptor system appears to be a common regulator for all types of endothelial cells in the body. Very recently, a tissue-specfic endothelial cell regulator, **EG-VEGF**, has been isolated. The VEGF family and this new type endothelial cell regulator are important for our understanding of the molecular basis of physiological as well as pathological angiogenesis.

L2 ANSWER 39 OF 39 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN

1996:265591 The Genuine Article (R) Number: UC787. Dermal papilla cells from human hair follicles secrete factors (**eg VEGF**) mitogenic for endothelial cells. Hibberts N A (Reprint); Kato S; Messenger A G; Randall V A. UNIV BRADFORD, DEPT BIOMED SCI, BRADFORD BD7 1DP, W YORKSHIRE, ENGLAND; ROYAL HALLAMSHIRE HOSP, DEPT DERMATOL, SHEFFIELD S10 2JF, S YORKSHIRE, ENGLAND. JOURNAL OF INVESTIGATIVE DERMATOLOGY (APR 1996) Vol. 106, No. 4, pp. 341-341. ISSN: 0022-202X. Publisher: BLACKWELL SCIENCE INC, 238 MAIN ST, CAMBRIDGE, MA 02142. Language: English.

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L5 ANSWER 1 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN
2004:780858 Document No. 141:273369 Compositions comprising human and mouse Bv8 and **EG-VEGF** with hematopoietic and immune activity and therapeutic uses for blood diseases and immune disorders. **Ferrara, Napoleone**; Lecouter, Jennifer (Genentech, Inc., USA). PCT Int. Appl. WO 2004081229 A2 20040923, 161 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2004-US7622 20040312. PRIORITY: US 2003-2003/PV45446U 20030312; US 2003-2003/PV511390 20031014.

AB The present invention relates to the novel expression and activities of Bv8 and **EG-VEGF** in hematopoietic stem cells (HSCs), lineage-committed blood progenitor cells, and lymphocytes. In particular, Bv8, **EG-VEGF**, and their receptors are expressed in bone marrow HSCs, peripheral blood leukocytes (PBLs), as well as many hematol. malignant cell lines. Bv8 and **EG-VEGF** are capable of promoting colony formation of bone marrow mononuclear cells and spleen-derived progenitor cells, increasing populations of white blood cells, and promoting activation of B lymphocytes and T lymphocytes. BvS8 nucleic acids and polypeptides, **EG-VEGF** nucleic acids and polypeptides, or combinations thereof can be used in a number of assays and in diagnosis and treatment of conditions associated with hematopoiesis, neutropenias, immunodeficiency disorders, and autoimmune disorders.

L5 ANSWER 2 OF 17 MEDLINE on STN DUPLICATE 1
2004599383. PubMed ID: 15548611. Bv8 and endocrine gland-derived vascular endothelial growth factor stimulate hematopoiesis and hematopoietic cell mobilization. LeCouter Jennifer; Zlot Constance; Tejada Max; Peale Franklin; **Ferrara Napoleone.** (Department of Physiology, Genentech, Inc., South San Francisco, CA 94080, USA.. lecouter@gene.com) . Proceedings of the National Academy of Sciences of the United States of America, (2004 Nov 30) 101 (48) 16813-8. Electronic Publication: 2004-11-17. Journal code: 7505876. ISSN: 0027-8424. Pub. country: United States. Language: English.

AB Bv8 and endocrine-gland-derived VEGF (**EG-VEGF**), or prokineticins, are two highly related, secreted proteins that we previously described as selective angiogenic mitogens. Here we describe the expression and functional characterization of Bv8 in peripheral blood cells, notably monocytes, neutrophils, and dendritic cells, and in the bone marrow. In human and mouse, the two Bv8 G protein-coupled receptors are expressed in hematopoietic stem cells and specific mature blood cells, including lymphocytes. Bv8 is highly expressed by neutrophils at sites of inflammation and can stimulate migration of monocytes, in a pertussis toxin-sensitive manner. Bv8, or **EG-VEGF** that shares the same receptors, increased numbers of colony-forming units granulocytic and monocytic in cultures of human or mouse hematopoietic stem cells.

Systemic in vivo exposure to Bv8 or **EG-VEGF** resulted in significant increases in total leukocyte, neutrophil, and monocyte counts. Additionally, adenovirus (Av)Bv8 or AvEG-VEGF delivered just before 5-fluorouracil injury promoted the survival of hematopoietic cells and enhanced progenitor mobilization. In conclusion, Bv8 can promote survival and differentiation of the granulocytic and monocytic lineages. Bv8 potentially modulates growth, survival, and function of cells of the innate and adaptive immune systems, possibly through autocrine or paracrine signaling mechanisms.

L5 ANSWER 3 OF 17 MEDLINE on STN DUPLICATE 2

2004388609. PubMed ID: 15292351. Human endocrine gland-derived vascular endothelial growth factor: expression early in development and in Leydig cell tumors suggests roles in normal and pathological testis angiogenesis. Samson Michel; Peale Franklin V Jr; Frantz Gretchen; Rioux-Leclercq Nathalie; Rajpert-De Meyts Ewa; **Ferrara Napoleone.** (Department of Molecular Oncology, Genentech, Inc., South San Francisco, California 94080, USA.) Journal of clinical endocrinology and metabolism, (2004 Aug) 89 (8) 4078-88. Journal code: 0375362. ISSN: 0021-972X. Pub. country: United States. Language: English.

AB Angiogenesis is essential for tumor growth and metastasis. A new human angiogenic mitogen, endocrine gland-derived vascular endothelial growth factor (**EG-VEGF**), has been recently identified; its expression pattern is restricted to endocrine glands, with the highest expression in testis. We used in situ hybridization and newly generated monoclonal antibodies to investigate the expression of **EG-VEGF** in normal human prenatal and adult testis and in 48 human testicular tumors of different subtypes. We found that **EG-VEGF** was expressed from 14 wk until birth in human fetal testis. In the adult testis, **EG-VEGF** was strongly expressed only in Leydig cells. In testicular tumors, **EG-VEGF** was expressed specifically in Leydig cell tumors, whereas germ cell-derived neoplasms, including carcinoma in situ, seminoma, and nonseminomatous germ cell tumors, were negative for this antigen. In contrast, VEGF, another powerful angiogenic factor, was expressed in seminoma, but very weakly in Leydig cell tumors. Interestingly, we found that Leydig cell tumors presented vessel surface density 3.2-fold higher than seminoma. These findings argue that human **EG-VEGF** may play a role in angiogenesis both during the early endocrine development of testis and in the adult testis as well as in Leydig cell tumor growth.

L5 ANSWER 4 OF 17 MEDLINE on STN DUPLICATE 3

2004095079. PubMed ID: 14984768. **EG-VEGF** and Bv8: a novel family of tissue-restricted angiogenic factors. **Ferrara Napoleone**; LeCouter Jennifer; Lin Rui; Peale Franklin. (Department of Molecular Oncology, Genentech Inc, South San Francisco, CA 94080, USA.. nf@gene.com) . Biochimica et biophysica acta, (2004 Mar 4) 1654 (1) 69-78. Ref: 82. Journal code: 0217513. ISSN: 0006-3002. Pub. country: Netherlands. Language: English.

AB A novel family of angiogenic mitogens have been recently characterized. Endocrine gland-derived vascular endothelial growth factor (**EG-VEGF**), and the mammalian homologue of Bombina variegata peptide 8 (Bv8), are two highly related endothelial cell mitogens and chemotactic factors with restricted expression profiles and selective endothelial cell activity. These peptides share two cognate G-protein coupled receptors. The expression of human **EG-VEGF** occurs predominantly in steroidogenic glands. Consistent with such an expression pattern, the human **EG-VEGF** gene promoter has a potential binding site for steroidogenic factor (SF)-1, a pivotal element for steroidogenic-specific transcription. In the human ovary, the expression of **EG-VEGF** is temporally and spatially complementary to the expression of VEGF-A, both in the follicular and in the luteal phase, suggesting complementary and coordinated roles of these molecules in ovarian angiogenesis. Also, **EG-VEGF** expression

correlates with vascularity in the polycystic ovary syndrome, a leading cause of infertility. Bv8 expression is mainly restricted to the testis. The identification of these tissue-selective angiogenic factors raises the possibility that other secreted molecules with selectivity for the endothelium of other organs exist.

L5 ANSWER 5 OF 17 MEDLINE on STN DUPLICATE 4
2004255671. PubMed ID: 15153419. **EG-VEGF**: a novel mediator of endocrine-specific angiogenesis, endothelial phenotype, and function. Lecouter Jennifer; Lin Rui; **Ferrara Napoleone.** (Department of Molecular Oncology, Genentech Inc., South San Francisco, California 94080, USA.) Annals of the New York Academy of Sciences, (2004 Apr) 1014 50-7. Ref: 69. Journal code: 7506858. ISSN: 0077-8923. Pub. country: United States. Language: English.
AB Angiogenesis is the focus of therapeutic efforts to promote new vessel development in damaged tissues. Conversely, inhibiting endothelial cell growth and survival is a strategy to treat various proliferative diseases. Much evidence indicates that VEGF is a key mediator of angiogenesis. Recently, a novel angiogenic mitogen with tissue-specific expression and target selectivity was characterized. Human endocrine gland derived vascular endothelial growth factor (**EG-VEGF**) is selectively expressed in steroidogenic glands and promotes growth of endocrine gland endothelium. The identification of tissue-selective angiogenic factors raises the possibility that other secreted molecules in this class exist. The potential advantage of tissue-specific angiogenic therapeutics may be the reduction of systemic side effects. Additionally, these peptides or their receptors may be attractive targets for inhibition in several disorders.

L5 ANSWER 6 OF 17 MEDLINE on STN DUPLICATE 5
2003106208. PubMed ID: 12604792. The endocrine-gland-derived VEGF homologue Bv8 promotes angiogenesis in the testis: Localization of Bv8 receptors to endothelial cells. LeCouter Jennifer; Lin Rui; Tejada Max; Frantz Gretchen; Peale Franklin; Hillan Kenneth J; **Ferrara Napoleone.** (Department of Molecular Oncology, Genentech, Inc., South San Francisco, CA 94080, USA.) Proceedings of the National Academy of Sciences of the United States of America, (2003 Mar 4) 100 (5) 2685-90. Electronic Publication: 2003-02-25. Journal code: 7505876. ISSN: 0027-8424. Pub. country: United States. Language: English.
AB We recently identified an angiogenic mitogen, endocrine-gland-derived vascular endothelial growth factor (**EG-VEGF**), with selective activity for endothelial cells of endocrine tissues. Here we describe the characterization of a highly related molecule, Bv8, also known as prokineticin-2. Human Bv8 shares 60% identity and 75% similarity with **EG-VEGF.** The human and mouse Bv8 genes share a common structure. Like **EG-VEGF**, Bv8 is able to induce proliferation, survival and migration of adrenal cortical capillary endothelial cells. Bv8 gene expression is induced by hypoxic stress. Bv8 expression occurs predominantly in the testis and is largely restricted to primary spermatocytes. Adenoviral delivery of Bv8 or **EG-VEGF** to the mouse testis resulted in a potent angiogenic response. We have localized the expression of the Bv8EG-VEGF receptors within the testis to vascular endothelial cells. The testis exhibits relatively high turnover of endothelial cells. Therefore, Bv8 and **EG-VEGF**, along with other factors such as VEGF-A, may maintain the integrity and also regulate proliferation of the blood vessels in the testis.

L5 ANSWER 7 OF 17 MEDLINE on STN DUPLICATE 6
2003223990. PubMed ID: 12746324. Mouse endocrine gland-derived vascular endothelial growth factor: a distinct expression pattern from its human ortholog suggests different roles as a regulator of organ-specific angiogenesis. LeCouter Jennifer; Lin Rui; Frantz Gretchen; Zhang Zemin; Hillan Kenneth; **Ferrara Napoleone.** (Department of Molecular Oncology, Genentech Inc., South San Francisco, California 94080, USA.)

Endocrinology, (2003 Jun) 144 (6) 2606-16. Journal code: 0375040. ISSN: 0013-7227. Pub. country: United States. Language: English.

AB We recently described human endocrine gland-derived vascular endothelial growth factor (**EG-VEGF**) as an endothelial cell mitogen with a novel selective activity and an expression pattern essentially limited to steroidogenic glands. Herein we present the identification and characterization of the mouse ortholog. The mouse cDNA and predicted amino acid sequences are, respectively, 86% and 88% identical with the human. Surprisingly, the mouse **EG-VEGF** transcript is predominantly expressed in liver and kidney. A comparison of human and mouse **EG-VEGF** promoter sequences revealed a potential binding site for NR5A1, which is known to be a pivotal element for steroidogenic-specific transcription, in the human but not mouse promoter. In situ hybridization studies localized expression of mouse **EG-VEGF** mRNA to hepatocytes and renal tubule cells. Interestingly, capillary endothelial cells in these sites share several common structural features with those found in steroidogenic glands. Within liver and kidney, **EG-VEGF** receptor expression was largely restricted to endothelial cells. Mouse **EG-VEGF** promoted proliferation and survival of endothelial cells. We propose that mouse **EG-VEGF**, like human **EG-VEGF**, plays a role in regulating the phenotype and growth properties of endothelial cells within distinct capillary beds.

L5 ANSWER 8 OF 17 MEDLINE on STN DUPLICATE 7

2003235306. PubMed ID: 12759245. Differential expression of the angiogenic factor genes vascular endothelial growth factor (VEGF) and endocrine gland-derived VEGF in normal and polycystic human ovaries. **Ferrara Napoleone**; Frantz Gretchen; LeCouter Jennifer; Dillard-Telm Lisa; Pham Thinh; Draksharapu Aparna; Giordano Thomas; Peale Franklin. (Department of Molecular Oncology, Genentech Incorporated, South San Francisco, California 94080, USA.) American journal of pathology, (2003 Jun) 162 (6) 1881-93. Journal code: 0370502. ISSN: 0002-9440. Pub. country: United States. Language: English.

AB Angiogenesis is a key aspect of the dynamic changes occurring during the normal ovarian cycle. Hyperplasia and hypervascularity of the ovarian theca interna and stroma are also prominent features of the polycystic ovary syndrome (PCOS), a leading cause of infertility. Compelling evidence indicated that vascular endothelial growth factor (VEGF) is a key mediator of the cyclical corpus luteum angiogenesis. However, the nature of the factor(s) that mediate angiogenesis in PCOS is less clearly understood. Endocrine gland-derived (**EG**)-**VEGF** has been recently identified as an endothelial cell mitogen with selectivity for the endothelium of steroidogenic glands and is expressed in normal human ovaries. In the present study, we compared the expression of **EG-VEGF** and VEGF mRNA in a series of 13 human PCOS and 13 normal ovary specimens by in situ hybridization. **EG-VEGF** expression in normal ovaries is dynamic and generally complementary to VEGF expression in both follicles and corpora lutea. A particularly high expression of **EG-VEGF** was detected in the Leydig-like hilus cells found in the highly vascularized ovarian hilus. In PCOS ovaries, we found strong expression of **EG-VEGF** mRNA in theca interna and stroma in most of the specimens examined, thus spatially related to the new blood vessels. In contrast, VEGF mRNA expression was most consistently associated with the granulosa cell layer and sometimes the theca, but rarely with the stroma. These findings indicate that both **EG-VEGF** and VEGF are expressed in PCOS ovaries, but in different cell types at different stages of differentiation, thus suggesting complementary functions for the two factors in angiogenesis and possibly cyst formation.

L5 ANSWER 9 OF 17 MEDLINE on STN DUPLICATE 8

2003461872. PubMed ID: 14522467. **EG-VEGF** and Bv8. a novel family of tissue-selective mediators of angiogenesis, endothelial phenotype, and function. LeCouter Jennifer; **Ferrara Napoleone.**

(Department of Molecular Oncology, Genentech Inc., 1 DNA Way, South San Francisco, CA 94080, USA.) Trends in cardiovascular medicine, (2003 Oct) 13 (7) 276-82. Ref: 80. Journal code: 9108337. ISSN: 1050-1738. Pub. country: United States. Language: English.

AB Angiogenic molecules are the focus of therapeutic efforts to promote new vessel development in ischemic or damaged tissue and, conversely, to inhibit endothelial cell growth and survival in proliferative disease. Two novel angiogenic mitogens have been characterized recently. Endocrine gland-derived vascular endothelial growth factor (**EG-VEGF**) and the mammalian homologue of Bombina variegata peptide 8 (Bv8) are endothelial cell mitogens and chemotactic factors with restricted expression profiles and selective endothelial cell activity. These highly related peptides share two cognate G-protein-coupled receptors that are homologous to the neuropeptide Y receptor. The identification of tissue-selective angiogenic factors raises the possibility that other secreted molecules in this class exist. The potential advantage of tissue-specific angiogenic therapeutics may be the reduction of systemic side effects. Additionally, these peptides or their receptors may be attractive targets for inhibition in several disorders.

L5 ANSWER 10 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN

2002:10528 Document No. 136:65270 Protein and cDNA sequences encoding human **EG-VEGF** protein and methods of use. **Ferrara, Napoleone; Watanabe, Colin; Wood, William I.** (Genentech, Inc., USA). PCT Int. Appl. WO 2002000711 A2 20020103, 133 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US20116 20010622. PRIORITY: US 2000-2000/PV21363U 20000623; US 2000-2000/PV23097W 20000907; WO 2000-US32678 20001201.

AB The present invention is directed to novel polypeptides designated herein as **EG-VEGF** of human and to nucleic acid mols. encoding those polypeptides. Also provided herein are vectors and host cells comprising those nucleic acid sequences, chimeric polypeptide mols. comprising the polypeptides of the present invention fused to heterologous polypeptide sequences, antibodies which bind to the polypeptides of the present invention and to methods for producing the polypeptides of the present invention. Also provided herein are methods of screening for modulators of **EG-VEGF**. Furthermore, methods and related methods of treatment are described herein which pertain to regulating cellular proliferation and chemotaxis.

L5 ANSWER 11 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN

2002:964996 Document No. 138:33697 Endocrine gland-derived vascular endothelial growth factor nucleic acids and polypeptides and their biological activities and use in drug screening and therapies. **Ferrara, Napoleone; Watanabe, Colin; Wood, William I.**; Shek, Theresa (USA). U.S. Pat. Appl. Publ. US 2002192634 A1 20021219, 105 pp., Cont.-in-part of U.S. Ser. No. 886,242. (English). CODEN: USXXCO. APPLICATION: US 2001-27603 20011219. PRIORITY: US 1998-PV96146 19980811; WO 1999-US12252 19990602; US 1999-PV145698 19990726; US 1999-380137 19990825; WO 2000-US219 20000105; WO 2000-US4914 20000224; WO 2000-US8439 20000330; US 2000-PV213637 20000623; US 2000-PV230978 20000907; US 2000-709238 20001108; WO 2000-US32678 20001201; US 2001-886242 20010620.

AB The present invention is based on the identification and characterization of a novel, tissue-restricted, growth and differentiation factor that acts selectively on one endothelial cell type. This factor, referred to as endocrine gland-derived vascular endothelial growth factor (**EG-VEGF**), induces proliferation, migration, and fenestrations in

capillary endothelial cells derived from endocrine glands, but has no effect on a variety of other endothelial and non-endothelial cell types tested. **EG-VEGF** also induces phosphorylation of kinases involved in cell proliferation or survival, including ERK1, ERK2, Akt, and eNOS. **EG-VEGF** nucleic acids and polypeptides can be used in a number of assays and in diagnosis and treatment of conditions associated with hormone-producing tissue. Also provided herein are vectors and host cells comprising those nucleic acid sequences, chimeric polypeptide mols. comprising the polypeptides of the present invention fused to heterologous polypeptide sequences, antibodies which bind to the polypeptides of the present invention and to methods for producing the polypeptides of the present invention. Also provided herein are methods of screening for modulators of **EG-VEGF.** Furthermore, methods and related methods of treatment are described herein which pertain to regulating cellular proliferation and chemotaxis.

L5 ANSWER 12 OF 17 MEDLINE on STN DUPLICATE 9

2002139189. PubMed ID: 11751915. Characterization of endocrine gland-derived vascular endothelial growth factor signaling in adrenal cortex capillary endothelial cells. Lin Rui; LeCouter Jennifer; Kowalski Joe; **Ferrara Napoleone.** (Department of Molecular Oncology, Genentech Inc., South San Francisco, California 94080, USA.) Journal of biological chemistry, (2002 Mar 8) 277 (10) 8724-9. Electronic Publication: 2001-12-20. Journal code: 2985121R. ISSN: 0021-9258. Pub. country: United States. Language: English.

AB Endocrine gland-derived vascular endothelial growth factor (**EG-VEGF**) has been recently identified as a mitogen specific for the endothelium of steroidogenic glands. Here we report a characterization of the signal transduction of **EG-VEGF** in a responsive cell type, bovine adrenal cortex-derived endothelial (ACE) cells. **EG-VEGF** led to a time- and dose-dependent phosphorylation of p44/42 MAPK. This effect was blocked by pretreatment with pertussis toxin, suggesting that G alpha(i) plays an important role in mediating **EG-VEGF**-induced activation of MAPK signaling. The inhibitor of p44/42 MAPK phosphorylation PD 98059 resulted in suppression of both proliferation and migration in response to **EG-VEGF.** **EG-VEGF** also increased the phosphorylation of Akt in a phosphatidylinositol 3-kinase-dependent manner. Consistent with such an effect, **EG-VEGF** was a potent survival factor for ACE cells. We also identified endothelial nitric-oxide synthase as one of the downstream targets of Akt activation. Phosphorylation of endothelial nitric-oxide synthase in ACE cells was stimulated by **EG-VEGF** with a time course correlated to the Akt phosphorylation. Our data demonstrate that **EG-VEGF**, possibly through binding to a G-protein coupled receptor, results in the activation of MAPK p44/42 and phosphatidylinositol 3-kinase signaling pathways, leading to proliferation, migration, and survival of responsive endothelial cells.

L5 ANSWER 13 OF 17 MEDLINE on STN DUPLICATE 10

2003023758. PubMed ID: 12530695. Endocrine gland vascular endothelial growth factor (**EG-VEGF**) and the hypothesis of tissue-specific regulation of angiogenesis. **Ferrara Napoleone**; LeCouter Jennifer; Lin Rui. (Department of Molecular Oncology, Genentech Inc., South San Francisco, CA 94080, USA.. nf@gene.com) . Endocrine research, (2002 Nov) 28 (4) 763-4. Journal code: 8408548. ISSN: 0743-5800. Pub. country: United States. Language: English.

L5 ANSWER 14 OF 17 MEDLINE on STN DUPLICATE 11

2003329369. PubMed ID: 12858543. The role of **EG-VEGF** in the regulation of angiogenesis in endocrine glands. LeCouter J; Lin R; **Ferrara N.** (Department of Molecular Oncology, Genentech, Inc., South San Francisco, California 94080, USA.) Cold Spring Harbor symposia on quantitative biology, (2002) 67 217-21. Ref: 51. Journal code: 1256107. ISSN: 0091-7451. Pub. country: United States. Language: English.

L5 ANSWER 15 OF 17 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN DUPLICATE 12

2002:446084 Document No.: PREV200200446084. **EG-VEGF** and the hypothesis of tissue-specific regulation of angiogenesis. **Ferrara, Napoleone** [Reprint author]; LeCouter, Jennifer [Reprint author]; Lin, Rui [Reprint author]. Dept Molecular Oncology, Genentech Inc, South San Francisco, CA, USA. Biology of Reproduction, (2002) Vol. 66, No. Supplement 1, pp. 82. print.
Meeting Info.: 35th Annual Meeting of the Society for the Study of Reproduction. Baltimore, Maryland, USA. July 28-31, 2002.
CODEN: BIREBV. ISSN: 0006-3363. Language: English.

L5 ANSWER 16 OF 17 MEDLINE on STN DUPLICATE 13

2002233229. PubMed ID: 11969366. **EG-VEGF** and the concept of tissue-specific angiogenic growth factors. LeCouter Jennifer; **Ferrara Napoleone.** (Department of Molecular Oncology, Genentech, 1 DNA Way, South San Francisco, CA 94080, USA.) Seminars in cell & developmental biology, (2002 Feb) 13 (1) 3-8. Ref: 68. Journal code: 9607332. ISSN: 1084-9521. Pub. country: England: United Kingdom. Language: English.

AB The endothelium of the vascular beds is extremely diverse and exquisitely distinct with respect to the specific tissue compartment served by the vessels. The molecular identity and function of the instructive signals that tailor the tissue-specific endothelial phenotype have been largely undefined. Presumably, a complex, integrated network of signals derived from the tissue parenchyma and/or stromal compartments is responsible. Recently, we identified a novel angiogenic mitogen, endocrine-gland-derived vascular endothelial growth factor, **EG-VEGF**, with a selective activity and very distinct expression pattern. Human **EG-VEGF** is expressed by steroid producing cells in the adrenal gland, placenta, testis and ovary, and is a mitogen for endothelial cells derived from these microvascular beds. **EG-VEGF** may represent the first of a novel class of tissue-specific angiogenic factors that function to regulate and fine-tune endothelial cell growth, structural and functional properties. The identification of other selective angiogenic molecules will allow insight into exciting, basic developmental issues and increase our armamentarium of factors for therapeutic angiogenic and anti-angiogenic strategies.

L5 ANSWER 17 OF 17 MEDLINE on STN DUPLICATE 14

2001486108. PubMed ID: 11528470. Identification of an angiogenic mitogen selective for endocrine gland endothelium. LeCouter J; Kowalski J; Foster J; Hass P; Zhang Z; Dillard-Telm L; Frantz G; Rangell L; DeGuzman L; Keller G A; Peale F; Gurney A; Hillan K J; **Ferrara N.** (Department of Molecular Oncology, Genentech Inc., South San Francisco, CA 94080, USA.) Nature, (2001 Aug 30) 412 (6850) 877-84. Journal code: 0410462. ISSN: 0028-0836. Pub. country: England: United Kingdom. Language: English.

AB The known endothelial mitogens stimulate growth of vascular endothelial cells without regard to their tissue of origin. Here we report a growth factor that is expressed largely in one type of tissue and acts selectively on one type of endothelium. This molecule, called endocrine-gland-derived vascular endothelial growth factor (**EG-VEGF**), induced proliferation, migration and fenestration (the formation of membrane discontinuities) in capillary endothelial cells derived from endocrine glands. However, **EG-VEGF** had little or no effect on a variety of other endothelial and non-endothelial cell types tested. Similar to VEGF, **EG-VEGF** possesses a HIF-1 binding site, and its expression is induced by hypoxia. Both **EG-VEGF** and VEGF resulted in extensive angiogenesis and cyst formation when delivered in the ovary. However, unlike VEGF, **EG-VEGF** failed to promote angiogenesis in the cornea or skeletal muscle. Expression of human **EG-VEGF**

messenger RNA is restricted to the steroidogenic glands, ovary, testis, adrenal and placenta and is often complementary to the expression of VEGF, suggesting that these molecules function in a coordinated manner. **EG-VEGF** is an example of a class of highly specific mitogens that act to regulate proliferation and differentiation of the vascular endothelium in a tissue-specific manner.

```
=> s l3 and "VRPA"
L6            0 L3 AND "VRPA"

=> s l3 and PRO1186
L7            3 L3 AND PRO1186

=> dup remove l7
PROCESSING COMPLETED FOR L7
L8            3 DUP REMOVE L7 (0 DUPLICATES REMOVED)

=> d l8 1-3 cbib abs
```

L8 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2005 ACS on STN

2002:773696 Document No. 137:289998 Cloning, protein and cDNA sequence of human protein **PRO1186.** Baker, Kevin; Chen, Jian; Goddard, Audrey; Gurney, Austin L.; Smith, Victoria; **Watanabe, Colin K.**; **Wood, William I.**; Yuan, Jean (Genentech, Inc., USA). Eur. Pat. Appl. EP 1247863 A1 20021009, 49 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL. (English). CODEN: EPXXDW. APPLICATION: EP 2002-12968 19990602. PRIORITY: US 1998-PV96146 19980811; EP 1999-955293 19990602.

AB The invention relates to protein and cDNA sequence of human protein **PRO1186.** The invention relates to methods and vector for recombinant expression of protein **PRO1186** in mammalian cell, yeast, Escherichia coli and insect cell. The invention relates to antibody against protein **PRO1186** and drug screening.

L8 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2005 ACS on STN

2001:417147 Document No. 135:29838 Secreted and transmembrane proteins identified by sequence comparison and cDNAs encoding them and their uses. Baker, Kevin; Beresini, Maureen; Deforge, Laura; Desnoyers, Luc; Filvaroff, Ellen; Gao, Wei Qiang; Gerritsen, Amry E.; Goddard, Audrey; Godowski, Paul J.; Gurney, Austin L.; Gherwood, Steven; Smith, Victoria; Stewart, Timothy A.; Tumas, Daniel; **Watanabe, Colin K.**; **Wood, William I.**; Zhang, Zemin (Genentech, Inc., USA). PCT Int. Appl. WO 2001040466 A2 20010607, 813 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2000-US32678 20001201. PRIORITY: WO 1999-US28301 19991201; WO 1999-US28551 19991202; WO 1999-US28565 19991202; WO 1999-US30095 19991216; WO 1999-US30999 19991220; WO 1999-US31274 19991230; WO 2000-US277 20000106; WO 2000-US3565 20000211; WO 2000-US4342 20000218; WO 2000-US4914 20000224; WO 2000-US5601 20000301; US 2000-PV187202 20000303; WO 2000-US6884 20000315; WO 2000-US7532 20000321; WO 2000-US13705 20000517; WO 2000-US14941 20000530; US 2000-PV209832 20000605; WO 2000-US22031 20000811; WO 2000-US23328 20000824; WO 2000-US30952 20001108.

AB The present invention is directed to novel polypeptides and to nucleic acid mols. encoding those polypeptides. Also provided herein are vectors and host cells comprising those nucleic acid sequences, chimeric polypeptide mols. comprising the polypeptides of the present invention fused to heterologous polypeptide sequences, antibodies which bind to the

polypeptides of the present invention and to methods for producing the polypeptides of the present invention. The proteins show overexpression in cancer and may of diagnostic use. Certain of the proteins were found to form complexes with one another.

L8 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2005 ACS on STN
2000:881316 Document No. 134:37955 Methods and compositions for inhibiting neoplastic cell growth with utilization of chimeric polypeptides of PRO184 and **PRO1186**. Ashkenazi, Avi J.; Hillan, Kenneth J.; Napier, Mary A.; **Watanabe, Colin K.; Wood, William I.** (Genentech, Inc., USA). PCT Int. Appl. WO 2000075327 A1 20001214, 104 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 2000-US4914 20000224. PRIORITY: WO 1999-US12252 19990602; US 1999-PV145698 19990726; WO 2000-US219 20000105.

AB The present invention concerns methods and compns. for inhibiting neoplastic cell growth. In particular, the present invention concerns antitumor compns. and methods for the treatment of tumors. The invention further concerns screening methods for identifying growth inhibitory, e.g., antitumor compds. The present invention is directed to novel polypeptides and to nucleic acid mols. encoding those polypeptides which include human PRO184 and **PRO1186**. These proteins were effectively expressed in Escherichia coli and yeast and mammalian cells and baculovirus cells. Also provided herein are vectors and host cells comprising those nucleic acid sequences, chimeric polypeptide mols. comprising the polypeptides of the present invention fused to heterologous polypeptide sequences, antibodies which bind to the polypeptides of the present invention and to methods for producing the polypeptides of the present invention. The expressed PRO184 and **PRO1186** proteins may include or exclude their signal peptides or extracellular domains. These antibodies may be humanized or monoclonal. This involves the utilization of an epitope tag. In situ hybridization was employed to detect **PRO1186** gene expression in ovarian cortical stroma and in leydig cells of testis. Applications for drug screening and rational drug design are described in addition to a labeled container and package insert describing the effect. Here, an antitumor assay involving antiproliferation is described. Applications for treatment of breast cancer, ovarian cancer, renal cancer, colorectal cancer, uterine cancer, prostate cancer, lung cancer, bladder cancer, CNS cancer, melanoma and leukemia are all described.

```
=> s "VRPA"
L9            5 "VRPA"

=> dup remove l9
PROCESSING COMPLETED FOR L9
L10           2 DUP REMOVE L9 (3 DUPLICATES REMOVED)

=> d l10 1-2 cbib abs
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L10 ANSWER 1 OF 2 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN DUPLICATE 1
2000219131 EMBASE Evaluation of radiation absorption in slurry photocatalytic reactors. 2. Experimental verification of the proposed method. Brandi R.J.; Alfano O.M.; Cassano A.E.. A.E. Cassano, Inst. Desarrollo Tecn. Indust. Quim., Universidad Nacional del Litoral, CONICET, Guemes 3450, 3000 Santa Fe, Argentina. acassano@alpha.arcride.edu.ar. Environmental Science and Technology Vol. 34, No. 12, pp. 2631-2639 15 Jun 2000.

Refs: 9.
ISSN: 0013-936X. CODEN: ESTHAG
Pub. Country: United States. Language: English. Summary Language: English.
ED Entered STN: 20000713
AB The volume-averaged volumetric rate of photon absorption (**VRPA**) in a photocatalytic reactor has been experimentally determined by measuring the radiative fluxes coming into and going out of the reaction space through the glass walls of a reactor. These radiative fluxes were obtained from experimental measurements made with precisely calibrated UV detectors. These values of the volume-averaged **VRPA** were used to decide the validity of theoretical calculations obtained from the rigorous application of the radiative transfer equation. Afterward, the reaction kinetic dependence with respect to the local volumetric rate of photon absorption (LVRPA) and its effect on the quantum yield evaluation were analyzed. To do this, the linear and square root reaction rate dependencies with the LVRPA were considered. Employing a titanium dioxide suspension, it has been demonstrated that (i) failing to properly account for radiation scattering in suspended solid photocatalytic reactors will normally lead to significant errors in the evaluation of the true absorbed light and (ii) point values of the photon absorption rate are necessary in order to represent the true kinetics of the photocatalytic reaction. The reason being the existence of very strong spatial nonuniformities in the above-mentioned rates.

L10 ANSWER 2 OF 2 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN
1991:477193 The Genuine Article (R) Number: GC019. VARIATIONAL RANDOM PHASE APPROXIMATION USING THE ONE-COMPONENT-PLASMA REFERENCE. IWAMATSU M (Reprint). CHIBA KEIZAI UNIV, TODOROKI CHO 3-59-5, CHIBA 260, JAPAN (Reprint). PHYSICS LETTERS A (5 AUG 1991) Vol. 157, No. 6-7, pp. 415-418. ISSN: 0375-9601. Publisher: ELSEVIER SCIENCE BV, PO BOX 211, 1000 AE AMSTERDAM, NETHERLANDS. Language: English.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB We propose a simplified variational random phase approximation (**VRPA**) for the structure factor of liquid alkali metals using the one-component-plasma (OCP) reference. Our formulation combines the standard random phase approximation (RPA) for the structure factor with the variational form of the mean spherical approximation (MSA) for the reference system. Our formula is similar to the optimized random phase approximation (ORPA), but can avoid the introduction of the fictitious hard core to the reference system. Application of the method to liquid Na and K indicates that the accuracy of this method is comparable with the ORPA using the hard sphere reference.

```
=> s black mamba venom protein A
L11           0 BLACK MAMBA VENOM PROTEIN A

=> s venom
L12      103455 VENOM

=> s l12 and protein A
L13         321 L12 AND PROTEIN A

=> s l13 and black mamba
L14          10 L13 AND BLACK MAMBA

=> dup remove l14
PROCESSING COMPLETED FOR L14
L15            2 DUP REMOVE L14 (8 DUPLICATES REMOVED)

=> d l15 1-2 cbib abs

L15 ANSWER 1 OF 2      MEDLINE on STN                    DUPLICATE 1
1999349621.     PubMed ID: 10422759.   Bv8, a small protein from frog skin and
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its homologue from snake **venom** induce hyperalgesia in rats. Mollay C; Wechselberger C; Mignogna G; Negri L; Melchiorri P; Barra D; Kreil G. (Institute of Molecular Biology, Austrian Academy of Sciences, Salzburg.) European journal of pharmacology, (1999 Jun 18) 374 (2) 189-96. Journal code: 1254354. ISSN: 0014-2999. Pub. country: Netherlands. Language: English.

AB From skin secretions of Bombina variegata and Bombina bombina, we isolated a small protein termed Bv8. The sequence of its 77 amino acids was established by peptide analysis and by cDNA cloning of the Bv8 precursor. Bv8 stimulates the contraction of the guinea-pig ileum at nanomolar concentrations. The contraction is not inhibited by a variety of antagonists. Injection of a few micrograms of Bv8 into the brain of rats elicits, as assessed by the tail-flick test and paw pressure threshold, a marked hyperalgesia which lasts for about 1 h. Bv8 is related to **protein A**, a component of the **venom** of the **black mamba**. After i.c.v. injection, **protein A** is even more active than Bv8 in inducing hyperalgesia.

L15 ANSWER 2 OF 2 MEDLINE on STN DUPLICATE 2

81115818. PubMed ID: 7461607. Snake **venom**. The amino acid sequence of **protein A** from Dendroaspis polylepis polylepis (**black mamba**) **venom**. Joubert F J; Strydom D J. Hoppe-Seyler's Zeitschrift fur physiologische Chemie, (1980 Dec) 361 (12) 1787-94. Journal code: 2985060R. ISSN: 0018-4888. Pub. country: GERMANY, WEST: Germany, Federal Republic of. Language: English.

AB **Protein A** from Dendroaspis polylepis polylepis **venom** comprises 81 amino acids, including ten half-cystine residues. The complete primary structures of **protein A** and its variant A' were elucidated. The sequences of **proteins A** and A', which differ in a single position, show no homology with various neurotoxins and non-neurotoxic proteins and represent a new type of elapid **venom** protein.

```
=> s "TANGO"
L16         716 "TANGO"

=> s l16 and Tie Ligand
L17           0 L16 AND TIE LIGAND

=> s l16 and VEGF
L18           0 L16 AND VEGF

=>

---Logging off of STN---


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COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                 ENTRY     SESSION
FULL ESTIMATED COST                             129.09      129.30

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)    SINCE FILE      TOTAL
                                                 ENTRY     SESSION
CA SUBSCRIBER PRICE                             -11.68      -11.68

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